A CASE OF "SPLENOMEGALIC" OR "MYELOPATHIC" POLYCYTHÆMIA, WITH TRUE PLETHORA AND ARTERIAL HYPERTONIA, WITHOUT CYANOSIS

BY

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[*From Volume 88 of the 'Medico-Chirurgical Transactions'*]

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Received February 25th, 1905; Read May 9th, 1905.

In the absence of cyanosis the following case differs from the cases of chronic cyanosis with polycythæmia and splenomegaly recorded by Vaquez, Saundby and Russell, Rosengart, Osler, and others. I have had the advantage of being able to study a typical example of such cases,[1] and believe that the present case is really of the same nature but at an earlier stage, and occurring in a fairly robust subject whose circulatory system is acting efficiently. I would temporarily include all these cases, with or without cyanosis, under one heading, namely, "Splenomegalic polycythæmia," although I think it possible that the spleen need not be obviously enlarged to clinical examination in all cases. In many respects cases of this group, like the present one—that is to say, cases with-

[1] F. Parkes Weber and J. H. Watson, "Chronic Polycythæmia with Enlarged Spleen," 'Transactions of the Clinical Society of London,' 1904, vol. xxxvii, p. 115; and 'International Clinics,' 1905, vol. iv, p. 47.

out cyanosis—resemble the case of "hypertonia polycythæmica" (Geisböck) recently recorded by Hess,[1] but apparently differ from it in the absence of albuminuria and the presence of splenomegaly.

The present patient, a Jewish woman, aged 37, of medium height and weight, first came under my care in July, 1903, for acute erythromelalgia of the left foot.[2] This condition under rest in bed and other treatment became less acute, and finally gradually disappeared.

The existence of the polycythæmia was first detected when the blood was examined in March, 1904, but was probably present earlier. From April, 1904, to February, 1905, the patient was constantly under observation in the German Hospital, and on April 22nd, 1904, was shown at a Clinical evening of the Clinical Society. Owing to the disappearance of the erythromelalgia she is no longer confined to her bed. In fact, the condition for which she originally came under treatment is practically cured, though her other symptoms, objective and subjective, persist, and it is with these that the present paper deals.

There is no distinct cyanosis of the face, though the cutaneous blood-vessels are somewhat over-filled, and the tongue is generally of a bright red colour with a bluish tinge resembling the colour of raw butcher's meat. The toes, especially of the left foot, sometimes appear rather livid, but this is possibly connected with the past erythromelalgia, which, it should be remembered, was not entirely confined to the left foot. No evidence of disease has been discovered in the heart or lungs. There is no dyspnœa. By examination of the abdomen nothing abnormal can be detected excepting moderate enlargement of the spleen, which can be felt, one or two finger-breadths below the ribs. For diagnostic purposes, owing to a question of the possibility of splenic tuberculosis, Koch's

[1] Abstract by Pappenheim in the 'Folia Hæmatologica,' 1905, vol. ii, p. 47. *Cf.* F. Geisböck, 'Verhandl. d. XXI Kongresses f. inn. Med.,' 1904, p. 97.

[2] I described this part of the case in the 'British Journal of Dermatology,' February, 1904, p. 70.

old tuberculin was employed in December, 1904, but the injection of five milligrammes failed to produce a reaction. Menstruation regular. Bowels sometimes confined. The urine is usually rather pale, acid, of low specific gravity (about 1010), somewhat increased in quantity, and free from albumen and sugar. The percentage of urea has not been regularly estimated. On one occasion it was 1·9 per cent., making the total daily excretion up to or somewhat above the average. The body weight on June 21st, 1904, was 10 st. 6 lbs.: on August 23rd it was 10 st. 10 lbs.; on November 21st it was 11st.; on February 6th, 1905, it was 11 st. 2 lbs. Slight enlargement of the thyroid gland was temporarily noticed in October, 1904. There is considerable deafness in both ears, possibly connected with chronic dry catarrh. The patient's subjective symptoms consist in a disagreeable noise in her ears and occasionally headaches and slight vertigo, also apparently feelings of prostration. The noise in her head is always present, but varies in character from a whizzing or rushing to a roaring or rumbling sound, and is rhythmical with the heart's action.

I will now give an account of the examination of the blood and circulatory system whilst the patient has been under observation.

Circulatory system.—As already mentioned, nothing abnormal has been found by physical examination of the heart, the apex beat being in the fifth left intercostal space, internal to the nipple line, and the area of cardiac dulness not being increased. The pulse at the wrist is of medium volume and increased tension; it is regular, the rate being about 80—90 in the minute, but affected by mental excitement. Pulse tracings made with a Dudgeon's sphygmograph in June, 1904, showed a pulse of high tension. On December 20th, 1903, Hill and Barnard's pocket sphygmometer on the radial artery gave the blood-pressure as about 140 mm. Hg. (that is, the pressure at which the oscillations were greatest), but their larger instrument on the arm showed a pressure of about 165 mm. Hg. On

December 16th, 1904, Dr. Haldane kindly estimated the maximum brachial blood-pressure by Martin's modification of the Riva Rocci apparatus, and found it to be 157 mm. Hg., and on January 21st, 1905, he found it 152 mm. Hg. In June, 1904, Dr. Gruber kindly made an ophthalmoscopic examination of the blood-vessels in the fundus oculi and reported that the veins were markedly congested and slightly tortuous, but the macular region did not show any decided enlargement of capillaries such as he had noted in the case of chronic cyanosis and polycythæmia[1] already alluded to.

The blood.—The following table is intended to show the results of blood counts[2] and microscopic examination of the blood in relation to diet and treatment from March, 1904, to February, 1905. It must be remembered that, owing to the improvement in the condition of the left lower extremity, the patient was able to be up and to get about much more at the end of this period than at the beginning, and this may have exercised an influence on the general condition.

In addition to the drugs mentioned on the table, bromides, aspirin, and valerian were sometimes used. At the commencement of July, 1904, minute doses of calomel were tried for about a week, but without any obvious effect on the general condition.

The red cells and hæmoglobin value.—The red cells varied abnormally in size, and, according to Dr. Boycott, in shape and staining capacity. These changes, together with the

[1] Weber and Watson, *loc. cit.*

[2] The blood counts were made by a Thoma-Zeiss hæmocytometer, and the hæmoglobin value was obtained either by a Gowers' hæmoglobinometer or by Haldane's modification. In the latter estimations (November 30th and later) either a correct Haldane's instrument was used or an old Gowers' instrument freshly standardised by the kindness of Dr. Haldane and Dr. A. E. Boycott. The instruments used in the earlier estimations were not freshly standardised. I had the pipette of a Gowers' hæmoglobinometer graduated so that only half the usual amount of blood might be sucked up. In this way the diluted blood does not rise above the scale.

presence of a few nucleated red cells, might, as Dr. Boycott points out, be ascribed to unusual activity in the erythroblastic functions of the bone marrow. The nucleated reds seen were all normoblasts, and in the blood-films from November 30th, 1904, as many as three were noticed during a differential count of 500 white cells; in the blood from December 16th eleven normoblasts were found on two

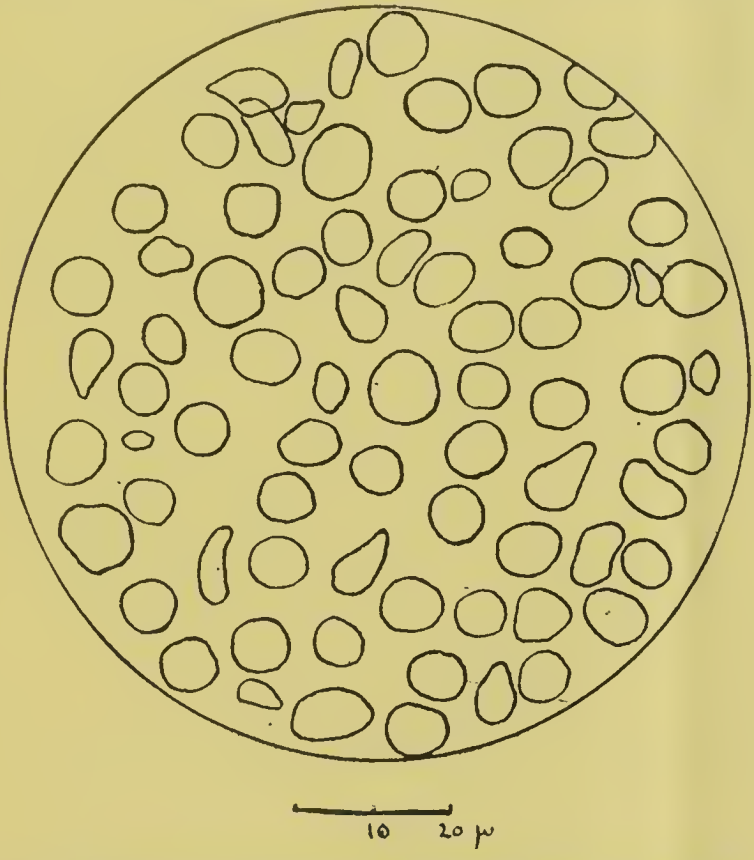

FIG. 1.—Red blood corpuscles, showing variations in size and shape, in a film taken on August 15th, 1904. Drawn to scale by Dr. A. E. Boycott.

slides in the course of a search of about three quarters of an hour. Erythroblasts have likewise been observed by Türk and some others in cases of splenomegalic polycythæmia. In regard to the occasional presence of nucleated red cells in normal human blood, Dr. Boycott tells me that though probably present in all persons they are

Date.	Hæmoglobin per cent. of normal standard.	Red cells per c.mm.	White cells per c.mm.	Polymorpho-nuclears per cent.	Small lymphocytes per cent.	Large lymphocytes, large mononuclears, and "transitionals" per cent.	Coarsely granular eosinophiles per cent.	Mast-cells per cent.	Erythroblasts (all normoblasts).
1904 April 13th	120	8,240,000	6000	73·75	17·25	8·5	0·5	Only one seen	—
April 17th	125	9,440,000	8100	—	—	—		—	—
April 19th	—	8,660,000	9000	77·6	18·5	3·5	0·3	—	—
May 30th	165	10,600,000	7200	68·8	26·5	4·0	0·7	—	—
June 12th	170	—	—	—	—	—	—	—	—
June 20th	148	10,960,000	8800	—	—	—	—	—	—
July 8th	175	9,440,000	8400	—	—	—	—	—	—
Aug. 3rd	148	8,016,000	8000	—	—	—	—	—	—
Aug. 15th	177	9,840,000	—	77·0	13·0	8·0	0·4	1·6	Present

Average diameter of erythrocytes.	Diet and Treatment.	Remarks.
—	—	The differential count was of 400 white cells by Dr. G. L. Eastes. During the count one mast cell was found. No myelocytes or erythroblasts. Three or four of the white cells counted were "intermediate forms," and Dr. Eastes enumerated these with the type which they most resembled.
—	—	—
—	At the end of April, 1904, a milk diet was ordered, but was only continued for a few days owing to the patient's objection to it. She was then put on ordinary meat diet, and from May 9th was given two to three drops of liquor arsenicalis three times daily. The arsenic was discontinued on May 30th	This blood-count was made by Dr. J. H. Drysdale when he kindly came to see the patient. The large lymphocytes were counted with the small lymphocytes as "lymphocytes." I have, therefore, included them in the group of small lymphocytes; Dr. Drysdale is not responsible for this.
Not greater than the normal.	—	Dr. G. L. Eastes made the differential count and reported that no myelocytes or erythroblasts were seen, and that there was no poikilocytosis. Films were likewise sent to Prof. H. Vaquez, who mentioned in his paper with Dr. Laubry that they confirmed his opinion that in splenomegalic polycythæmia there was no hyperglobuly, that is to say, increase in the average diameter of 100 red cells, though microcytes and macrocytes might be present.
Great variety in size noted	—	—
—	At the end of June, 1904, meat was discontinued, and the diet was made to consist of milk, milk puddings, bread, butter, potatoes, green vegetables, and stewed fruit, with every day two eggs, and about twice weekly some fish. From July 8th, 1904, till Feb., 1905, she took the juice of one lemon daily	Prof. A. E. Wright kindly took away specimens of the blood and urine for examination (*see* later). His count made the red blood corpuscles just over 11,000,000 in the c.mm., a result not very different from that of the count at the hospital.
—	—	—
—	—	This count was taken after unusually copious menstruation.
7·48 μ	—	The differential count was of 500 white cells by Dr. A. E. Boycott. He found the average diameter of 50 red cells to be 7·48 μ; maximum diameter, 8·57 μ; minimum diameter, 5·95 μ.

Date.	Hæmoglobin per cent. of normal standard.	Red cells per c.mm.	White cells per c.mm.	Polymorpho-nuclears per cent.	Small lymphocytes per cent.	Large lymphocytes, large mononuclears, and "transitionals" per cent	Coarsely granular eosinophiles per cent.	Mast-cells per cent.	Erythroblasts (all normoblasts).
1904									
Aug. 26th	177	9,680,000	6000	—	—	—	—	—	—
Sept. 9th	175	9,850,000	6000	—	—	—	—	—	—
Sept. 29th	185	9,800,000	—	—	—	—	—	—	—
Oct. 14th	184	9,968,000	7320	—	—	—	—	—	—
Nov. 16th	177	9,976,000	8320	—	—	—	—	—	—
Nov. 30th	156	8,480,000	8200	81·0	12·6	5·6	0·6	0·2	Several
Dec. 9th	—	—	—	73·0	15·0	8·4	3·0	0·6	Several
Dec. 16th	158	—	—	72·6	14·0	7·0	1·0	0·4	Several
Dec. 23rd	161	9,280,000	4800	—	—	—	—	—	—
1905									
Jan. 3rd	156	8,625,000	7500	75·4	18·6	5·4	0·6	Present	Present
Jan. 12th	145	9,568,000	6000	66·0	25·4	6·6	2·0	Present	Present
Jan. 21st	148	8,568,000	4000	75·0	11·0	11·6	2·0	0·4	Present
Feb. 6th	164	8,680,000	4800	80·4	14·0	4·0	1·0	0·6	Present

Average diameter of erythrocytes.	Diet and Treatment.	Remarks.
—	—	In August it was noted that patient could walk about without the left foot becoming hot or different in colour from the right foot.
—	—	The specimen of blood from which this count was made was obtained direct from a superficial vein in the right fore-arm by a Pravaz syringe.
—	In Sept. the diet was changed so as to include fish or meat every day at the mid-day meal. From Sept. 15th to Oct. 8th Röntgen ray treatment was carried out; 21 sittings of 5 to 10 minutes' exposure of the splenic region; at several sittings the lower parts of the legs were likewise exposed for 5 minutes	—
—	—	—
—	From Oct. 31st to Dec. 5th, 1904, three grains of potassium iodide were given three times daily	—
7·74 μ	—	The blood examination is by Dr. A. E. Boycott. During the differential count of 500 white cells he found 3 normoblasts, one with polychromatic cytoplasm and about 12 polychromatic red cells. The red cells varied from 4 μ to 10 μ in diameter, and there were too many oval and irregular shapes. The hæmoglobin was estimated by Dr. Haldane (*see* also later).
—	—	The red cells Dr. Boycott said showed the same abnormal variation in size, shape, and staining capacity as at the last examination. He soon found several normoblasts and some polychromatic red cells.
—	—	The hæmoglobin estimation was by Dr. Haldane.
—	Venesection 100 c.c.	The blood examination was of blood obtained by venesection containing 1 per cent. of a 50 per cent. aqueous solution of potassium citrate.
—	During last days of Dec. till Jan. 12th patient was taking 15 grs. of potassium bromide and 7½ grs. of aspirin thrice daily. From Jan. 12th till Feb. 6th, 1905, she took 10 grs. of sodium salicylate thrice daily	The differential counts in 1905 were all of 500 white cells, by Dr. A. E. Boycott, as were all the others from Nov. 30th. Dr. Haldane estimated the hæmoglobin on Jan. 21st. In the blood-films of Feb. 6th Dr. Boycott thought the changes in the red cells were much less marked than before, and could only discover one normoblast with great difficulty.
—		
7·6 μ		
—		

extremely rare. During the winter 1903–1904 he searched about 500 blood-films with this point in view, and only found three or four altogether, though 500 leucocytes were counted in each specimen.

The hæmoglobin values of the blood noted in April, 1904, were relatively low; probably the colour index of the corpuscles, and perhaps their size also, increased soon after this. The highest hæmoglobin values recorded were on October 14th, 1904 (184 per cent.), and on September 29th (185 per cent.), but the hæmoglobinometers used on these occasions had not been specially standardised. The recent figures have varied from 145 to 164 per cent. The hæmocytometer readings have on the whole varied less than the hæmoglobinometer readings. The largest number of red cells recorded was 10,960,000 on June 20th, 1904, and the lowest was 8,016,000 on August 3rd; at present (February 6th, 1905) there are about eight and a half millions in the cubic millimeter, and the average colour index of the cells is nearly up to the normal.

Vaquez[1] is probably right in saying that in splenomegalic polycythæmia, even when combined with marked cyanosis, there is no "hyperglobuly"—that is, that the average size of the red cells, judged by their average diameter, does not exceed normal limits. In my last case[2] it did not, and in the present case it does not; for Dr. Boycott estimated the average diameter at 7·7 μ on November 30th, 1904, and at 7·6 μ on January 21st, 1905.[3] In an old preparation from August 15th, 1904, he made it only about 7·5 μ. In this connection it is interesting that Professor A. E. Wright,[4] who kindly examined the patient's blood on June 20th, 1904, counted the red cells as just over 11,000,000 in the cubic millimetre, and

[1] Vaquez, "Du volume des globules rouges dans les polyglobulies avec cyanose." Société de Biologie, Paris, July 16th, 1904.

[2] *See* Weber and Watson, *loc. cit.* The average diameter was 7·1 μ.

[3] Dr. Boycott used ordinary stained blood-films for this purpose, measuring fifty to one hundred cells on each occasion.

[4] On the volumetric estimation of the corpuscular elements, *see* A. E. Wright, 'Lancet,' January 23rd, 1904, p. 216.

in the sedimentation tube obtained 9·25 volumes instead of the ordinary five volumes of corpuscles in ten volumes of blood. It may here be recalled that J. A. Capps in his 'Study of Volume Index'[1] concluded that the volume of the individual erythrocyte is best obtained by using the centrifuge in conjunction with the hæmocytometer.

The white cells.—In regard to the white cells the first thing to be noticed is the relative leucopenia, which has lately been very pronounced, the count having been on three occasions as low as four to five thousand in the cubic millimetre of blood. Relative leucopenia has, however, not been a feature in all cases of splenomegalic polycythæmia. The second point is the high percentage of polymorphonuclears, 66 to 81 per cent. This, Dr. Boycott thinks, forms additional evidence of unusual activity in the bone marrow. In my previous case of splenomegalic polycythæmia[2] the polymorphonuclears constituted 82·4 per cent. of the total white cells, and Vaquez[3] found the proportion 79 to 82 per cent. No myelocytes were found in the blood from either of my cases.

Total volume of the blood.—Dr. Haldane kindly came three times to estimate the total quantity of the patient's blood by his carbon monoxide method.[4] After his last visit he wrote that not only was there no doubt at all as to the enormous increase in the red corpuscles and hæmoglobin, but that he also felt convinced that the last blood-volume-determination (January 21st, 1905) left no loophole of error as to there being also a large increase in the blood-volume, though not so large as in many cases of chlorosis according to Dr. Lorrain Smith's estimations. Following are Dr. Haldane's figures of his first determination, November 30th, 1904, and of his third determination, January 21st, 1905. He

[1] 'Journal of Medical Research,' Boston, December, 1903, vol. x, p. 367.

[2] Weber and Watson, *loc. cit.*

[3] Vaquez and Laubry, "Cyanose avec Splénomégalie et Polyglobulie," 'Tribune Médicale,' Paris, August 13th, 1904, p. 517.

[4] *Vide* J. Haldane and J. Lorrain Smith, "The Mass and Oxygen Capacity of the Blood in Man," 'Journal of Physiology,' August 29th, 1900, vol. xxv, p. 331.

thinks there was certainly an error in his second determination December 9th, 1904, which has, therefore, been omitted.

Date.	Value of CO in c.c. at 0° C. and 760 mm barometric pressure.	Saturation of haemoglobin per cent.	Total oxygen capacity of blood in c.c.	Percentage of haemoglobin.[1]	Total volume of blood in c.c.[2]	Red corpuscles in c.mm. of blood.	White corpuscles in c.mm. of blood.	Body weight in kilos (clothes allowed for).	C.c. of blood per 100 grammes body weight.	Oxygen capacity per 100 grammes body weight in c.c.
1904 Nov. 30	74·0	4·6	1610	156	5600	8,480,000	8200	68	8·2	2·4
1905 Jan. 21	127·0	7·0	1810	148	6000	8,568,000	4000	68	9·7	2·7

The residue of carbon monoxide was analysed after each experiment to ascertain its degree of purity, and the air left in the bladder was also analysed to make certain that the carbon monoxide had been actually absorbed.

Amount of iron in the blood.—Some blood (45¾ grammes), after serving for the viscosity and cryoscopy examinations, was used by Mr. J. H. Ryffel, B.Sc., to obtain a quantitative estimation of the iron. He dried the blood in a platinum dish in the water oven, then ignited in the dish, till all carbon was burnt away, dissolved the ash in strong hydrochloric acid, diluted, filtered, evaporated in a porcelain dish with a few drops of strong nitric acid, redissolved in dilute hydrochloric acid, precipitated with ammonia, filtered, washed, dissolved in dilute sulphuric acid, reduced with pure zinc, filtered through asbestos, and titrated with $\frac{N}{10}$ permanganate solution. Mr. Ryffel found that the percentage of iron, calculated for the undiluted blood, was

[1] The normal percentage of hæmoglobin is reckoned as 100. It may be added that 100 c.c. of blood with this normal percentage of hæmoglobin can take up 18·5 c.c. oxygen.

[2] The normal individual is estimated to possess 4·6 c.c. of blood per 100 grammes body weight.

0·0673 grammes per cent. Dr. Boycott points out that supposing hæmoglobin to contain 0·33 grammes per cent. iron, Mr. Ryffel's result would correspond to 23·9 grammes hæmoglobin per cent. in the blood; the 100 per cent. of Haldane's hæmoglobinometer standard corresponds to an oxygen capacity of 18·5 per cent., which is believed to be equivalent to 13·7 grammes hæmoglobin per cent. in the blood; Mr. Ryffel's result would, therefore, correspond to 174 per cent. hæmoglobin on Haldane's scale. The hæmoglobin actually found in the venesection blood was 161 per cent. Allowing, therefore, for a little iron in the white blood corpuscles (normal blood-plasma is said to be free from iron) and for some evaporation (concentration of the blood) during the viscosity estimation, Mr. Ryffel's estimation of the total iron in the blood corresponds with the percentage of hæmoglobin found.

Specific gravity of the blood.—On June 27th, 1904, the specific gravity of a sample of the patient's blood obtained by pricking the finger was found to be 1·078, by the help of Hammerschlag's method. By the more accurate (pyknometer) weighing method the specific gravity of the blood obtained at the venesection on December 23rd, 1904 (after being mixed with 1 per cent. of a 50 per cent. aqueous solution of potassium citrate), was found to be 1·072.

Viscosity of the blood.—I made use of the citrated blood obtained at the venesection on December 23rd, 1904, to examine its viscosity by means of a viscosity tube exactly similar to the one suggested to me by Professor Arthur Schuster and made for me by Messrs. Baird and Tatlock, which I had employed with Dr. J. H. Watson in 1904[1] to ascertain the influence of the proportion of corpuscles on the viscosity of blood (in blood from a horse citrated to hinder coagulation). I found that the citrated blood from the patient took 203 seconds to run through the bulb of the tube, from one mark to the other, water taking only

[1] *Vide* Weber and Watson, 'Clin. Soc. Trans.,' 1904, vol. xxxvii. The apparatus used is described and figured on page 131.

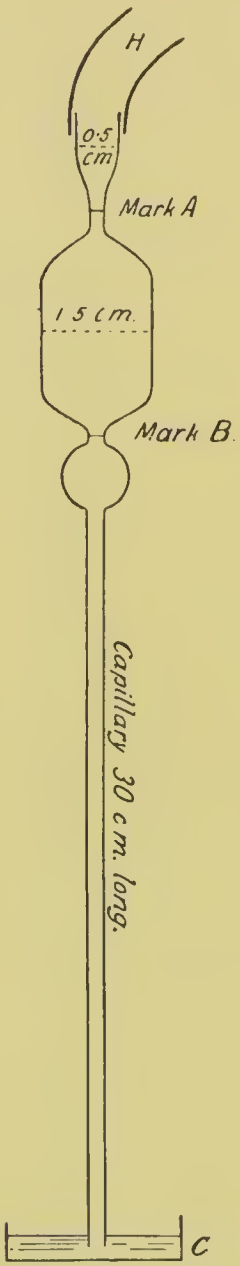

FIG. 2.—The blood is sucked up from an open vessel, C, by means of an india-rubber tube, H. The liquid is then allowed to fall whilst the tube is kept in a vertical position. The times at which the upper surface of the liquid passes the marks A and B are noted. If the time taken in two different liquids be t_1 and t_2 respectively, and p_1 and p_2 be the respective densities of the two liquids, and n_1 and n_2 their coefficients of viscosity, then $\frac{n_1}{n_2} = \frac{t_1 p_1}{t_2 p_2}$; so that, if for one liquid (as in our case for water), n_2 is known, n_1 may be calculated out.

19 seconds.[1] The specific gravity of the citrated blood was 1·072. Therefore, according to the formula given me by Professor Schuster, if n_1 = the coefficient of viscosity of the citrated blood and n = coefficient of viscosity of water at the temperature at which the experiment was made, $n_1 = \frac{n \times 203 \times 1{\cdot}072}{19 \times 1{\cdot}000}$. Therefore the coefficient of viscosity of the citrated blood was 11·45 times the coefficient of viscosity of the water used. Unfortunately, the temperature of the water used was not taken, and it may have been below the temperature of the room, which was about 18·4° C. Evidently, however, the viscosity of the blood was excessive, much higher than that of blood in ordinary diseases and conditions.

Cryoscopy of the blood.—Some blood obtained at the venesection on December 23rd, 1904 (mixed with 1 per cent. of a 50 per cent. aqueous solution of potassium citrate) was employed by Dr. Emery, Clinical Pathologist at King's College Hospital, to determine the freezing point, which he very kindly did on the day on which the blood was obtained. After the slight correction necessary for the presence of potassium citrate the freezing point was found to be minus 0·53° C., and therefore not very different to that of normal blood, which is about minus 0·56° C. The urine passed by the patient immediately after the venesection was of specific gravity 1008, faintly acid, and free from albumen and sugar. Dr. Emery found its freezing point was minus 0·79° C. Dr. Emery added that the blood plasma could not be collected in amount sufficient for the estimation of the freezing point, as after thorough centrifugalisation of a specimen of the citrated blood the plasma layer was only about 2 mm. thick, or, roughly speaking, only about 3 per cent. of the blood-column.

The salts in the blood and urine.—On June 20th, 1904,

[1] The tube previously used for the experiments with horse's blood was not used on this occasion, because water took about 44 seconds to run through the bulb, and the estimation of the viscosity of the patient's blood would have taken an unnecessarily long time.

Professor A. E. Wright[1] estimated the salts in the blood as equivalent to 0·58 per cent. sodium chloride (in lieu of the normal, about 0·78 per cent.), the salts of the urine[2] coming out as equivalent to 0·46 per cent. sodium chloride. This, Professor Wright says, gives an excretory quotient of about 0·8 instead of the normal of over 2·0. However, on June 26th, 1904, he estimated the salts in the blood-serum as equivalent to 1·14 per cent. sodium chloride, whilst the salts in the fluid from a blister were equivalent to 0·95 per cent. sodium chloride.

The alkalinity of the blood.—Professor Wright estimated this on June 26th, 1904, as equivalent to that of a normal alkaline solution diluted thirty-five times. He expresses it as $\frac{N}{35}$.

The amount of albuminous substance in the blood-plasma.—Professor Wright found the amount in the citrated blood obtained on December 23rd, 1904 (at the venesection) to be normal. His method of measuring the albuminous substances is by the resistance of the clot obtained by heating a graduated series of dilutions of the plasma.[3]

The coagulation of the blood.—Professor Wright thought its occurrence was very much delayed on June 20th, 1904. Afterwards it appeared to occur fairly readily, but the exact coagulation-time was not estimated.

The resistance of the red cells to hæmolytic agents.—Professor Wright examined the citrated blood from December 23rd, 1904, by a method of his own, and found the resistant power of the red cells to be about normal. One volume of centrifugalised sediment of red cells (the red cells were by repeated centrifugalisation washed fairly clean of blood-plasma) was suspended in sufficient $\frac{N}{10}$ salt

[1] *Vide* Wright and Kilner, "On a New Method of Testing the Blood and the Urine," 'Lancet,' April 2nd, 1904, p. 921.

[2] This was the urine passed directly after the examination of the blood, the bladder having been emptied before the examination. It was of specific gravity 1010, clear, rather pale, acid, and free from albumen.

[3] A. E. Wright, 'Lancet,' January 23rd, 1904, p. 218.

solution to bring the total volume of the suspension up to three volumes. Complete hæmolysis was then obtained by adding one volume of the suspension in a capillary tube to one volume of a $\frac{N}{30}$ salt solution.

Effect of Treatment and Progress of the Case.

As already stated, it is exceedingly difficult to estimate how much the patient's condition has really altered apart from the improvement in the erythromelalgic extremity. She can now walk about quite well, and has gained in weight, the erythromelalgia has disappeared, but the polycythæmia, high arterial tension, and the other phenomena in the blood and circulatory system persist, as do likewise the subjective symptoms (headache, etc.), although they vary in degree from time to time.

Arsenic, which was employed by W. Türk[1] in his cases, was soon discontinued in the present case on account of a considerable apparent increase in the number of red corpuscles which followed its use. On the whole, the patient has seemed to be better when on a diet containing relatively little meat, and when taking lemon-juice daily. It is possible that small doses of iodide of potassium or salicylates have a favourable influence. I have little doubt that absolute rest in bed, which was at one time required owing to the erythromelalgia, has an injurious influence on the general condition, and some of the slight apparent improvement in the general condition may be due to the patient having been able to take a little exercise (favouring metabolic processes). Opium and its derivatives have not been given a trial. In regard to drugs such as phenacetin and antifebrin (acetanilide) it must not be forgotten that the chronic use of antifebrin seems to give rise to cyanosis and blood changes.[2]

[1] 'Wiener klin. Wochenschrift,' 1904, Nos. 6 and 7.

[2] Stengel and White, "A Report of a Case of Chronic Acetanilide Poisoning, with marked Alterations in the Blood," 'University of Pennsylvania Medical Bulletin,' Philadelphia, February, 1903, p. 462.

The venesection in the present case seemed to make no difference in the subjective or objective condition, and it was not repeated, but perhaps the amount of blood (100 c.c.) withdrawn was too little to produce any decided change. It may be noted also that the diminution in the number of red blood corpuscles observed on August 3rd, 1904, followed unusually copious menstruation.

The employment of Röntgen rays, which has lately been found to have such a decided effect in many cases of leukæmia, seems to have made no change in the number of red blood corpuscles in the present case. This is not to be wondered at, since the action of these rays on the spleen and hæmopoietic tissues in leukæmia seems to be chiefly on the lymphocytes ("lymphocytolysis") and lymphadenoid tissues, and on the leucocytes generally ("leucolysis").[1] It is, however, to be noted that after a good many Röntgen ray sittings the patient complained more of headache or feeling of congestion in the head, and this decided us to discontinue the treatment. The number of white cells in the cubic millimetre has been particularly low at recent counts (see the table), and the spleen has not been so easy to feel. It is possible, therefore, that the Röntgen rays, though they had no influence on the number of red blood cells, may have had a slight tardy effect on the spleen and on the formation of white cells, analogous to that recorded in cases of leukæmia. The Röntgen ray treatment was carried out by Dr. Mülberger, senior house surgeon at the German Hospital, who employed apparatus of Siemens and Halske, of London, with direct street main supply; spark gap, 25 cm.; mercury dip break; 220 volts; 10 ampères; frequent breaks; hard tube (C. H. Müller, of Hamburg, No. 13 with vacuum-regulating apparatus); distance of the patient's skin from anticathode, 50 cm.; diaphragm compressor according to Dr. Faulhaber, of Würzburg. The splenic region was subjected to the treat-

[1] *Cf.* especially A. Wolff, "Theoretisches über die Behandlung der Leukämien und Anämien mit lytischen Methoden durch Röntgenstrahlen und leukolytische Sera," 'Wiener klin.-ther. Wochenschrift,' 1904, No. 49.

ment for five minutes at every sitting, and for one minute in addition every subsequent sitting till ten minutes were reached, after which the time of exposure was not changed. The treatment was carried out regularly, one sitting every day (Sundays excepted) from September 15th to October 8th, 1904, twenty-one sittings altogether. At nearly all of these sittings the lower parts of the legs were likewise exposed to the rays for five minutes.

In regard to future treatment it will be important to observe how the patient progresses now that she has left the hospital; in fact, the question is whether any special treatment is at present advisable or not. In the absence of all evidence that the disease is primary in the spleen, I do not think that the operation of splenectomy can be recommended.

Remarks and Conclusions.

As stated at the commencement of this paper, I regard the present case, in spite of the absence of cyanosis, as similar in nature to my previous case[1] of splenomegalic polycythæmia. The excess of red corpuscles, true plethora ("polyhæmia") and arterial hypertonia were present in both cases. In the previous case the polycythæmia, with the resulting increased viscosity of blood and increased strain on the circulatory mechanism, was, doubtless, of older standing, the patient's vital powers were probably on the decline, and the cyanosis and relatively scanty urine may have been a result of a gradually developing inadequacy of the circulatory mechanism to compensate for the great viscosity of the blood, in spite of the presence of high arterial blood-pressure.

The conclusions arrived at in my paper with Dr. J. H. Watson as to a pathological activity in the production of erythrocytes in the bone marrow being the cause of the blood and circulatory phenomena have, I think, been amply confirmed by the present case. Our theoretical observations on a possible alteration in the osmotic tension of the

[1] Weber and Watson, *loc. cit.*

blood may not have been required to explain the phenomena observed, and, indeed, I shall not discuss that question here, as I have no fresh evidence to offer that there is any special change in regard to osmotic tension to be found in the symptom-complex under consideration.

In my previous case the existence of most extensive bone-marrow changes was proved by examination after death. A great portion of the normal bone-marrow of the shafts of the long bones was found to have been replaced by red bone-marrow, relatively free from fat, in which very active formation of red corpuscles was in progress, as evidenced by the large quantity of erythroblasts. The changes were, however, not exclusively of an erythroblastic kind, and it may be doubted whether the erythrocyte-producing functions of the bone-marrow can ever be greatly increased without the myelocytes being to some extent involved in the unusual activity. Dr. Boycott has pointed out that in the present case an abnormal activity of the bone-marrow may not only account for the excess of red cells in the blood, for the great variations in their size (and for the variations noted in lesser degree, in their shape and staining capacity) and for the presence of nucleated red cells, but likewise for the high percentage of polymorphonuclear leucocytes. These changes have been found in other cases of splenomegalic polycythæmia.

There is no evidence pointing to diminished destruction or lessened wearing out of red blood cells as a factor in the production of the anomalous blood condition.

If the polycythæmia were due merely to concentration of the blood, it would doubtless be only temporary, and the blood would rapidly be diluted by fluid absorbed from the alimentary canal either directly into the blood-capillaries or else into the lacteals to be thrown into the blood-stream by way of the thoracic duct. Moreover, the fact that the total volume of blood in the body is abnormally great precludes the possibility that mere concentration of blood can be the cause of the blood changes. The clinical investigations of these blood changes, as already pointed

out, as well as post-mortem examination, show that in cases of splenomegalic polycythæmia there is increased production of red corpuscles, and I think the evidence is now really conclusive that the symptom-complex is always accompanied by, and at all events mainly due to, a pathological activity in the bone-marrow. Whether the latter condition can or cannot be regarded as the primary factor is a question to which I shall refer later on.

The objection to calling the symptom-complex "primary myelopathic polycythæmia" is that we are not sure that the disturbance of the bone-marrow is necessarily the primary pathogenic factor; whilst the term "myelogenic polycythæmia" is insufficient, for every polycythæmia, excepting temporary states due to mere concentration of the blood, and states (if there really are any) due to diminished destruction of erythrocytes, is "myelogenic" in the sense that the excess of red blood corpuscles is due to unusual activity of the bone-marrow. On the other hand, the term "splenomegalic polycythæmia" only signifies that the spleen is usually enlarged, not that it must necessarily be found enlarged in every case.

I now believe the *order of development of the main symptoms* and their *causal connection* to be as follows:

(1) Increased erythroblastic activity involving a great part, but not necessarily the whole, of the bone-marrow.[1]

(2) Increased viscosity of the blood resulting from the polycythæmia.

(3) Dilatation of small blood-vessels, partly to lessen resistance to the abnormally viscous blood, partly to make more room for dilution of the blood.

(4) The "plethora vera" or "polyhæmia" is probably to be regarded as an attempt to compensate for the

[1] In post-mortem investigations on these cases it would obviously, therefore, be a great mistake to be content with the examination of one portion of the bone-marrow. Part of the shaft of one long bone might be filled with bone-marrow of the ordinary yellow fatty variety, and yet the total active red-cell-forming bone-marrow in the body might be more than three times the normal amount.

increased viscosity of the blood and for the excessive percentage of the total blood-volume occupied by the cells. In fact, it is necessary, firstly, that there should be sufficient blood-plasma to nourish the tissues and make metabolism possible, and, secondly, that the viscosity may not become so great as to render sufficient circulation impossible.

(5) The arterial hypertonia is to be regarded as a result of the greater strain thrown on the circulatory mechanism.

(6) Cyanosis, when this occurs, is probably due to inadequacy of the series of compensatory changes, which, according to my view, precedes it.

In my opinion the evidence afforded by this and other cases strongly supports the foregoing conclusions, but the question now arises, *What is the nature of the pathological activity in the erythroblastic function of the bone-marrow?* At least two theoretical explanations suggest themselves. In the first place that the bone-marrow activity is a primary one, allied to a tumour formation, or the result of an "idiosyncrasy" of the patient. One can suppose, for instance, that some persons have a bone-marrow which reacts to ordinary erythroblastic stimuli to an excessive degree, viz. by throwing almost double the normal quantity of red cells into the blood-stream. If, however, as H. Ribbert[1] believes, there is a form of "myeloma" (that is to say, of growth originating in the elements of the bone-marrow) which should be termed "erythroblastoma," because the tumour-cells are related to erythroblasts, it seems possible that cases of splenomegalic polycythæmia, such as our two cases, may bear a relation to cases of erythroblastoma similar to that which lymphocytic leukæmia bears to lymphocytic myeloma.[2]

The other explanation is that some toxin of a hæmolytic

[1] H. Ribbert, 'Centralblatt für allg. Pathologie,' Jena, 1904, vol. xv, No. 9.

[2] *Cf.* F. Parkes Weber, "A Case of Acute Leukæmia, with a Scheme of Classification of Leukæmias and Pseudoleukæmias," 'Path. Soc. Trans.,' 1903, vol. liv, p. 286.

nature manufactured in the enlarged spleen or alimentary canal is absorbed into the circulating blood in minute quantities, not sufficient to cause much hæmolysis, but in amounts just sufficient to excite reaction in the hæmopoietic (erythroblastic) tissues. Metchnikoff quotes Belonovsky,[1] of St. Petersburg, as having increased both the number of corpuscles and the amount of hæmoglobin in the blood of anæmic persons by the injection of minute doses of hæmolytic serum.

I have just mentioned these possible alternatives in regard to the nature of the bone-marrow activity in splenomegalic polycythæmia, but they are merely theoretical suggestions, and I do not think it will be profitable to discuss them further without additional evidence.

The cause of the splenic enlargement.—If one inclines to the view that the bone-marrow condition in splenomegalic polycythæmia is the result of reaction to toxins circulating in the blood, it is natural to suggest that the enlargement of the spleen is due to the same toxins, whether they enter the circulation from the intestines or elsewhere, or else that there is a primary disease of the spleen, such as tuberculosis (as there actually was in the case of Rendu and Widal[2] and some other cases), which gives rise to a condition of toxæmia to which the bone-marrow reacts (excessive reaction being explained by idiosyncrasy) by an erythroblastic reaction resulting in polycythæmia. In favour of such a view there is the fact that in Saundby and Russell's case[3] of splenomegalic polycythæmia with cyanosis, Dr. Russell saw the patient with an enlarged spleen several years before cyanosis developed. To this I would answer that the polycythæmia was probably likewise present for years before the cyanosis developed, and that cyanosis, if the views I have brought forward are correct, is not an essential part of the symptom-complex.

[1] 'Sur l'Influence de l'Injèction de Diverses Doses de Sérum Hémolytique sur le Nombre des Elements du Sang,' St. Petersburg, 1902.

[2] 'Bulletins de la Soc. Médicale des Hôpitaux,' Paris, 1899, p. 528.

[3] "An Unexplained Condition of Chronic Cyanosis," 'Lancet,' 1902, vol. i, p. 515.

In my present case the enlargement of the spleen is not excessive, and does not appear to be progressive, and there is no fever or reaction to tuberculin to suggest the presence of tuberculosis. Splenic tuberculosis is certainly not necessarily present in cases of splenomegalic polycythæmia and primary tuberculosis of the spleen is not necessarily accompanied by polycythæmia.[1]

Possibly in the cases in which the splenic enlargement is due merely to increase of the pulp and engorgement with blood, as it seems to have been in my previous case, it may be explained as being due to the plethora vera (polyhæmia) and high blood-pressure, or as resulting from excessive functional activity in attempting to compensate for the excessive production of red corpuscles by increased destruction. Of these two last alternatives the former seems to me the most probable, as there is as yet no evidence of greatly increased destruction of red cells in these cases either occurring in the spleen or elsewhere.

Relation of erythromelalgia to polycythæmia.—There is no certain causal relationship, and in the present case the association of the two conditions may have been a chance one. Yet it must be remembered that the association of splenomegalic polycythæmia with erythromelalgia has already been noted by W. Türk,[2] of Vienna. I have elsewhere[3] given my reasons for believing that in the so-called "idiopathic or neuropathic erythromelalgia," as well as what might be termed "symptomatic erythromelalgia" (that is, severe pain and redness in an extremity affected with decided arterial obstruction), there is obstruction to the supply of arterial blood, at all events during the chronic stages. In the present case the muscular atrophy and absorption of bone-salts in the affected extremity[4] at

[1] *Cf.* J. Bayer, "Ueber die primäre Tuberkulose der Milz," 'Mitteil. aus den Grenzgebieten d. Med. u. Chir.,' 1904, vol. xiii, p. 523.

[2] 'Wiener Klinische Wochenschrift,' 1904, Nos. 6 and 7.

[3] 'British Journal of Dermatology,' February, 1904, p. 70.

[4] This was shown by radiograms of the two feet. *Vide* 'Clin. Soc. Trans.,' 1904, vol. xxxvii, p. 250.

one time pointed to local deficiency of arterial blood supply. It is possible that when for any reason the supply of blood to the bone-marrow of a long bone is greatly diminished the bone-marrow may make an attempt to manufacture more blood—in fact, may undergo a hæmopoietic (erythroblastic and leucoblastic) reaction. Through the kindness of my colleague, Dr. Michels, in 1904 I had the opportunity of examining the tibia removed by amputation from an extremity affected by chronic arterial obstruction. There was some red metaplasia of the bone-marrow at the ends of the shaft. In this case, however, the bone-marrow reaction may have been connected with the septic pyrexia preceding the amputation. Dr. J. Galloway also kindly showed me a patient with pain and redness in one foot, undoubtedly due to arterial obstruction, and informs me that in that patient the blood has been repeatedly examined, and the number of red cells has always been found considerably above the normal. Such an increase in the number of red blood corpuscles was, however, not present in another somewhat analogous case, and further information is needed to find out whether chronic ischæmia of an extremity, which can notoriously give rise to local muscular and osseous atrophy, can likewise produce changes in the bone-marrow of the affected part besides those due to absorption of fat-cells.

I have to thank all those who have so kindly assisted me in the examination of this case, without whose assistance I could not have arrived at my few conclusions—in the first place, Dr. J. Haldane, Dr. A. E. Boycott, and Prof. A. E. Wright, and then Dr. Drysdale, Dr. Emery, Mr. Ryffel and Dr. G. L. Eastes, and also (not least) the house physicians at the German Hospital, Dr. Blendinger and Schuh.

Literature.[1]

J. Bayer.—"Ueber die primäre Tuberkulose der Milz," 'Mitteil. aus den Grenzgebieten d. Med. u. Chir.,' Jena, 1904, vol. xiii, p. 523.

[1] This does not include all the articles referred to in the footnotes.

Xavier Bender.—"La Tuberculose de la Rate," 'Gazette des Hôpitaux,' Paris, March 31st, 1900, p. 375.

R. Breuer.—'Wiener Ges. für inn. Med.,' 1903; quoted by W. Türk.

R. C. Cabot.—"A Case of Chronic Cyanosis without discoverable Cause, ending in Cerebral Hæmorrhage," 'Boston Med. and Surg. Journ.,' December 7th, 1899, p. 574; "A second Case of Chronic Cyanosis without assignable Cause," *ibid.*, March 15th, 1900, p. 275.

Collet and Gallavardin.—"Tuberculose Massive Primitive de la Rate," 'Arch. de Med. Exp. et d'Anat. Path.,' Paris, 1901, vol. xiii, p. 191.

J. Collins.—"Chronic Cyanosis of the Extremities, associated with Polycythæmia and Splenomegaly," 'Medical Record,' New York, November 21, 1903, p. 807.

V. Cominotti.—"Hyperglobulie und Splenomegalie," 'Wiener Klin. Wochenschrift,' 1900, No. 39, p. 881.

G. A. Gibson.—"Adaptation and Compensation," 'Lancet,' December 5th, 1903, p. 1560; also "Some Observations on Cyanosis," 'Proc. Royal Soc. Edinburgh,' 1903, vol. xxiv, p. 393.

J. N. Hall, of Denver.—"Chronic Cyanotic Polycythæmia, with Notes upon two Cases," 'American Medicine,' Philadelphia, June 27th, 1903, p. 1026; quoted by J. Collins.

Hess.—"Ueber Hypertonia Polycythæmica," 'Med. Klinik,' 1905, vol. i; abstract by Pappenheim in 'Folia Hæmatologica,' 1905, vol. ii, p. 47.

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Kraus.—"Polycythämie mit Milztumor und Cyanose." This appeared in the Proceedings of the "Gesellschaft der Charité-Aerzte," 'Berliner klinische Wochenschrift,' March 13th, 1905, p. 307, after my paper was written.

S. F. McKeen.—"A Case of Marked Cyanosis, difficult to explain," 'Boston Med. and Surg. Journ.,' June 20th, 1901, p. 610.

R. Moutard-Martin and Lefas.—"Tuberculose primitive et massive de la Rate," 'Bulletins de la Soc. Médicale des Hôpitaux,' Paris, 1899, p. 547.

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J. Rosengart.—"Milztumor und Hyperglobulie," 'Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie,' Jena, 1903, vol. xi, p. 495.

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J. Scharold.—"Ein Fall von substantiver acuter Miliärtuberculose der Milz," 'Aerztliches Intelligenzblatt,' Munich, 1883, vol. xxx, p. 352.

D. D. Stewart.—"Acute Splenic Miliary Tuberculosis," 'Trans. Assoc. Amer. Physicians,' Philadelphia, 1901, vol. xvi, p. 431.

W. Türk, of Vienna.—"Beiträge zur Kenntniss des Symptomenbildes Polycythaemie mit Milztumor und Zyanose," 'Wiener Klinische Wochenschrift,' 1904, Nos. 6 and 7; also 'Wiener Ges. für inn. Med.,' 1902 and 1903.

H. Vaquez.—"Hyperglobulie et Splénomégalie," 'Bulletins de la Soc. Médicale des Hôpitaux,' Paris, 1899, p. 579; also "Sur une Forme spéciale de Cyanose s'accompagnant d'Hyperglobulie excessive et persistante," 'Comptes rendus de la Société de Biologie,' Paris, May 7th, 1892. A supplementary note ('Société Médicale des Hôpitaux,' Paris, January 25th, 1895) described the existence of splenomegaly and the absence of cardiac lesion in Vaquez's case. Chronic

polycythæmia with enlarged spleen might, therefore, almost be called "Maladie de Vaquez."

H. Vaques and Ch. Laubry.—"Cyanose avec Polyglobulie," 'Tribune Médicale,' Paris, August 13th, 1904, p. 517.

F. Parkes Weber and J. H. Watson.—"Chronic Polycythæmia with Enlarged Spleen," 'Clin. Soc. Trans.,' 1904, vol. xxxvii, p. 115; and 'International Clinics,' 1905, vol. iv, p. 47.

E. Weil.—"Note sur les organes hématopoiétiques et l'hématopoièse dans la cyanose congenitale," Société de Biologie, Paris, June 29th, 1901, p. 713.

Zaudy.—"Erythrozytose (Hyperglobulie) und Splenomegalie," 'Muenchener med. Wochenschr.,' July 5th, 1904, p. 1207.

ADDENDUM.

In cases of splenomegalic polycythæmia the onset of chronic cyanosis probably still further increases both the viscosity and the total volume of the blood. The effect of carbonic acid gas in increasing the viscosity of the blood has been clearly demonstrated by J. Bence ('Dent. Med. Wochenschrift,' April 13th, 1905, p. 590), who states also that, according to Limbeck, an increase in the total volume of the blood accompanies the increase in the viscosity, and adds that, according to Hamburger, this volumetric increase depends on an alteration in the osmotic relation between the red corpuscles and the blood-plasma.

Since writing the present paper, I have come across an interesting account, by W. Weintrand, of three cases of splenomegalic polycythæmia ('Zeitschrift f. klin. Medicin,' 1904, vol. lv, p. 91). The second of his patients suffered also from a condition said to resemble erythromelalgia. In the same case, on one occasion, a remarkable improvement in the subjective symptoms followed a sharp attack of hæmatemesis.

DISCUSSION.

Dr. J. S. HALDANE said that he wished first to congratulate Dr. Weber on the completeness of his investigation, which was evidently a piece of original work of great importance, and threw much new light on the subject. He thought that the facts recorded entirely bore out Dr. Weber's general conclusions as to the pathology of the disease. He did not think, however, that there was evidence of a plethora of blood-plasma. The proportion of plasma in the blood was clearly much diminished, so that in spite of the great increase in the total volume of the blood it might well be that the total volume of plasma was diminished rather than increased. When blood was injected from one animal into the vessels of another animal of the same species plasma rapidly disappeared, so that the percentage of red corpuscles for some time was greatly increased. The physiological tendency to keep the volume of the blood nearly constant seemed to overcome the tendency to keep the proportion of plasma to corpuscles normal, and this had probably occurred in the patient. With regard to the carbonic oxide method of measuring the total blood volume and total hæmoglobin in the body, he might perhaps mention that an experimental comparison of this method with the older method of Welcker (which, of course, implied killing the animal) was being carried out on animals by Mr. Gordon Douglas at the Oxford Physiological Laboratory. Although the investigation was not yet quite complete, the results attained showed that the two methods gave practically identical results. He would like to lay particular stress on the enormous excess in the total hæmoglobin contained in the blood of the patient. The hæmoglobin was most accurately measured in terms of its capacity for absorbing oxygen, and Professor Lorrain Smith and he had found that in normal men the oxygen capacity in c.c. per 100 grammes of body-weight was extraordinarily constant, and only varied in different individuals by about 10 per cent. from the average figure of 0·83 c.c. ('Journal of Physiology,' xxv, p. 340). In this patient the oxygen capacity was 2·7 c.c. There was thus an increase of more than 200 per cent. in the total hæmoglobin. Part of this hæmoglobin might be contained in the bone-marrow, outside the circulation, but in any case the result was very remarkable. Lorrain Smith and McKisack ('Path. Soc. Trans.,' 1902, liii, p. 136) had described a case of old pericarditis with cyanosis, in which the oxygen capacity was 2·0 c.c. In this case, however, the percentage of hæmoglobin was about normal, so that the increase in total hæmoglobin may have been primarily due to an increased blood-volume secondary to backward pressure and consequent increase in the capacity of the blood-vessels. He regretted that it had not been possible to give a fair trial to the therapeutic effects of bleeding the patient copiously, and possibly

repeatedly. By copious bleeding, repeated as often as necessary, it would undoubtedly be possible to keep the percentage of hæmoglobin normal, and he thought that probably the patient would benefit correspondingly. It must not, however, be forgotten that in the case of perfectly healthy individuals living at great altitudes, the percentage of hæmoglobin was commonly increased by about 40 or 50 per cent. without any apparent inconvenience occurring. Curiously enough, he had just received a letter on this subject from Mr. Richards, a Cornish mining engineer, who had recently gone out to manage a mine in Bolivia at an altitude of 15,000 feet, and had undertaken to make observations with a hæmoglobinometer, which had been carefully standardised at the Oxford Physiological Laboratory. His hæmoglobin had already, after a few weeks, risen gradually to 145 per cent., and his red corpuscles to 7,200,000, and he reported himself as feeling particularly well.

Dr. A. J. WHITING said there were many points in Dr. Parkes Weber's interesting paper which called for full discussion. He wished to refer to one. It was a little extraordinary that, although the adjectival term attached to the condition described was "splenomegalic," but little attention was given to the nature of the splenic enlargement present. There was no doubt that under certain circumstances the spleen had marked hæmopoietic functions. It was well known that normally during late intra-uterine and early extra-uterine life the spleen was a seat of the formation of red blood corpuscles. After bleeding animals copiously, the abstraction of blood being held to be an excitant of the hæmopoietic power of the body, the bone-marrow showed marked evidence of increased activity, but the same was also to be found in the spleen. His own experiments had been made mainly on dogs. The spleen in these animals became swollen, tense, of a rosy red colour, and more friable than natural after hardening. Microscopically, it showed large numbers of nucleated red cells, erythroblasts, and giant cells. Dr. Parkes Weber had referred to the presence of giant cells in the bone-marrow of his earlier cases; his own experience was that wherever blood-formation was taking place giant cells were to be found. In the spleens in question, while normally one or two might be seen in a section, after artificial hæmorrhage a thousand might be counted, and this seemed to offer a partial explanation of the mechanical increase in size of the organ. He had been interested to see that in regard to a recent case of leukæmia recorded abroad, in which large numbers of nucleated red cells were present in the blood, the author had said the splenic pulp was almost indistinguishable from the bone-marrow, and this was really so. He would like to ask if Dr. Parkes Weber had examined the spleen of his former case microscopically, and if so what were its characters?

Dr. A. E. Boycott, speaking from the point of view of the histology of the blood alone, considered that the condition described was a clinical entity. Apart from the increase in the hæmoglobin and in the number of cells he had found marked variation in size between individual red-blood corpuscles, their staining reactions were altered, and a small number of nucleated red-cells were constantly present. Polymorphonuclear neutrophile leucocytes were increased; this also indicated an increase in the activity of the bone-marrow.

[By permission of the President the two following letters, in the unavoidable absence of the writers, were admitted as contributions to the discussion.]

May 8th, 1905.

Dear Dr. Parkes Weber,—Let me thank you very warmly for your kindness in sending me the proof of the paper you are about to read to-morrow on "'Splenomegalic' or 'Myelopathic' Polycythæmia." When the subject first emerged, a few years ago, it seemed to me that it might be simply a form of cyanosis due to disturbance of the circulation by one of the many mechanical factors which may disturb the equilibrium. The consideration, however, of certain of the more recently published cases, the careful examination of an instance of the disease under the care of one of my friends here, which he recently published in the 'Edinburgh Medical Journal,'[1] and, above all, the study of your own work upon the subject, have led me to the conclusion that a purely mechanical hypothesis will not account for the phenomena. Your last paper has convinced me that increased blood-formation is the real cause of the disease, and I have no hesitation in accepting your suggestion of increased erythroblastic activity of the bone-marrow. Your conception of the order of development of the main symptoms appears to me to be perfectly correct, as increased viscosity of the blood must lead to increased strain on the circulation and to real plethora as an attempt to compensate for the viscosity.

G. A. Gibson.

Dear Dr. Parkes Weber,—A year and a half ago I had under my care at Westminster Hospital a case of splenomegalic polycythæmia, which presented many points of similarity with the case described in your paper.

The patient was a woman, aged 53, who had apparently been in good health until the time of the menopause, five years previously. At that time she had an attack similar to the one for which she was admitted to hospital, consisting of headache, vomiting, and giddiness, with marked weakness of all four limbs, lasting about a week; there was no loss of consciousness. In

[1] Ronaldson, 'Edin. Med. Journ.,' vol. xvi, 1904, p. 244.

about two months the patient appeared to recover completely. Three years before admission she had a second attack, similar to the first, but this time she was confined to the house for six months, and became permanently weak and unable to work. A year before admission she noticed a dragging pain in the left side of the abdomen, doubtless associated with the splenic enlargement. She noticed the abdomen to be red and swollen at this time. The pain passed off and did not recur.

Five weeks before admission the attack commenced for which she sought admission to hospital. It commenced with intense headache, dimness of vision, more marked in the right eye, and vomiting unassociated with food. Occasionally she noticed a little blood in the vomited material. She lost weight considerably during the five years of her illness.

On admission she was found to be somewhat emaciated; her lips were cyanosed, and the face had a dull, leaden flush, with dilated venules. The hands and feet were slightly red. The tongue and buccal mucosa were bright red. There was no dropsy or jaundice. She had numerous minute bright-red nævoid elevations, scattered over the skin of the trunk. Her skin was dry. No enlarged lymphatic glands could be detected anywhere. The heart was normal, save for some accentuation of the aortic second sound; the pulse was regular, of high tension and with thickened arterial walls. The superficial veins of the abdomen were markedly dilated and tortuous. The spleen was markedly enlarged, its notched border extending to one inch on the left of the umbilicus, the lower border reaching a level two inches below the umbilicus. The right lobe of the liver was also markedly enlarged and palpable, the vertical dulness extending from the fifth space in the nipple line to four inches below the costal margin. There was no ascites. The urine had a sp. gr. of 1024, was high-coloured, neutral in reaction, loaded with albumen, and microscopically showed granular, hyaline, and cell casts. There was double optic neuritis with retinal hæmorrhages. The nervous system at that time was otherwise normal. There was no tenderness of any of the long or flat bones, nor any joint affection. The blood was repeatedly examined by Dr. Hebb. It was very dark in colour, and of a viscous consistence. On October 23rd the erythrocytes were found to number 8,750,000 and the leucocytes 24,000 per cubic mm. (polymorphs 92 per cent., large monomorphs 2 per cent., small monomorphs 6 per cent.) On October 28th another count showed the red cells to number 10,333,000, the whites 23,400. The hæmoglobin was 130 per cent. The polymorphs were 94 per cent. granular (mostly finely granular), the monomorphs 6 per cent.

The patient left hospital against advice, and subsequently was admitted to Wandsworth Infirmary, where she died in April, 1904, five months after her admission to Westminster.

Shortly after she left Westminster she had an attack of right hemiplegia, with aphasia, apparently due to cerebral hæmorrhage. She gradually became totally blind in both eyes. The aphasia passed off, but the hemiplegia persisted. No autopsy could be obtained.

At the time when this patient was under my observation it was obvious that her case corresponded to the class described by Osler in the 'American Journal of the Medical Sciences' (August, 1903, p. 187). In connection with the erythromelalgia which has been noted by you in your case, my patient frequently observed that her hands and feet never felt cold, and they were certainly persistently flushed.

PURVES STEWART.

Dr. PARKES WEBER, in reply, said, in regard to Dr. Haldane's recommendation of very copious bleeding, that perhaps several smaller bleedings might be as effective as one large one, and would not be so terrifying. A single small bleeding may doubtless, however, be ineffectual. A few hours after one small bleeding in a patient (then under Dr. Weber's care) with chronic cyanosis, polycythæmia, and increased viscosity of blood, probably partly of pulmonary origin, an apparent increase in the number of red blood corpuscles was observed—that is to say, in the blood from pricking the finger as compared with the number in the venesection blood of a few hours previously. It seemed to be almost an impossibility to measure the amount of the plasma in the thick, sticky blood of extreme cases of polycythæmia, a great part of the plasma remaining, even after thorough centrifugalisation, in the interstices between the red corpuscles. In regard to Dr. Whiting's question, the enlargement of the spleen in his (Dr. Weber's) previous case of splenomegalic polycythæmia, which was examined microscopically, was due to increase in the ordinary splenic pulp, and largely, he thought, to engorgement of the organ with blood. He compared the myeloid transformation, mentioned by Dr. Whiting, in the spleen of animals rendered anæmic by repeated bleedings, to the myeloid change found in the spleen from a case of leukanæmia, which he had described in the 'Transactions' of the Pathological Society of London (1904, vol. lv, p. 287). In that case both the spleen and the liver were found to be crammed with erythroblasts and other cells of the bone-marrow kind (the liver containing numbers of giant cells), whilst the relatively small number of these bone-marrow elements present in the circulating blood during life made it probable that their presence in such great abundance in the spleen and liver after death was not merely the result of a metastasis or infiltration of these organs from the bone-marrow, but was to be regarded as representing a true myeloid transformation of the organs in question.

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